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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/718,102 | 11/20/2000 | Maria-Grazia Roncarolo | DX0261K1B | 9698 |

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| EXAMINER |
|---|
| HAMUD, FOZIA M |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | 18 |

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Final

| Office Action Summary | Application No. | Applicant(s) |
|---|---|---|
| | 09/718,102 | RONCAROLO ET AL. |
| | Examiner | Art Unit |
| | Fozia M Hamud | 1647 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-5 and 15-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 15-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

1. Receipt of Applicant's arguments and amendments filed in Paper No.17 on 29 April 2003 is acknowledged. Claims 2, 3, 5, 20, 25 and 27 have been amended. Claims 2-5 and 15-27 are pending and under consideration by the Examiner.

2. The following previous objections and rejections are withdrawn in light of Applicants amendments filed in Paper No.17, 04/29/03:

(I) The rejection of claim 2 made under 35 U.S.C. 112, first paragraph.

(II) The rejection of claim 5, made under 35 U.S.C. 112, second paragraph.

3. Applicant's arguments filed in Paper No.17, 04/29/03, have been fully considered but were deemed persuasive in part. The issues remaining are restated below.

***Claim Rejections-35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Applicants are thanked for understanding that the rejection of claim 23 was made under 35 U.S.C. 112, first paragraph (enablement), rather than under 35 U.S.C. 112, second paragraph, as the office action inadvertently indicated.

Applicants argue that the specification discloses the introduction of T cells to a recipient as well as administering IL-10 to a tissue to be transplanted, and points to page 5, lines 4-9 of the specification. Applicants also argue that there is no requirement to provide evidence of safety to satisfy the enablement requirement, since considerations made by the FDA are different from those made by PTO.

This argument has been fully considered but is not deemed persuasive. Applicants are correct in that the requirement of obtaining a patent is not the same as that of obtaining an FDA approval, however, the instant specification merely mentions that IL-10 and either an antigen or anti-CD3 antibodies are administered into a T cell, and then said T cell is introduced to a tissue transplantation recipient, but shows no data to support this speculation. Instant specification also states that IL-10 is administered to the tissue to be transplanted before transplantation, again without any data supporting this statement. Although working examples are not required under 35 U.S.C §112, first paragraph, they are one of the factors that must be considered when determining enablement, especially in light of the lack of guidance in the specification and the nature of the invention. While, expanding T cells ex-vivo and introducing them to a recipient might one day be a feasible therapy for tissue transplant patients, this type of therapy is still in early stages of research, and Applicants have not shown that it is effective and presictable. Also researchers continue to study various ways to fool the immune system into accepting foreign tissues or to take advantage of the immune response. Administration of IL-10 into the tissue to be transplanted might one day be a feasible therapy, however, this specification has not shown that this is an effective and predictable way of suppressing an immune response. Instant specification only speculates that the administration of IL-10 to a tissue to be transplanted might be an option for suppressing immune response that accompanies tissue transplantation, but provides no evidence that such is the case no guidance that it is predictable. Furthermore, although evidence is not a requirement to satisfy, 35 U.S.C. 112, first

paragraph, there has to be adequate guidance to render it predictable that the claimed invention would work. In the instant case, unless appropriate controls, are conducted, one of ordinary skill in the art would not have expected at the time instant case was filed, that administering IL-10 into a tissue transplantation recipient or to the tissue to be transplanted, would be an effective way of suppressing immune response.

Therefore, Applicants have not provided enablement for introducing T cells to a tissue transplantation recipient or administering IL-10 to the tissue to be transplanted prior to transplantation, as recited in claim 23.

***Claim Rejections-35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. The rejection of claims 2, 15 and 25-27 made under 35 U.S.C. 112, second paragraph is maintained.

5a. Claim 2 has been amended to recite "a method of inhibiting antigen-specific response of a T cell to subsequent presentation of said antigen, comprising administering to said *T cell* an effective....", however, it is unclear how IL-10 is administered to a T cell. It is unclear whether the T cell is in a subject, or whether it is in a laboratory dish.

5b. Claim 15 stands rejected under 35 U.S.C. 112, second paragraph for the reasons set forth in the previous office actions, because it is still unclear, how are the combination of IL-10 and either the antigen or anti-CD3 are administered into a T cell.

Again it is unclear, whether the T cell is *in-vivo* (i.e in a subject) or *in-vitro* (i.e in a petri dish).

Claims 3-5 and 16-24 are rejected as being vague and indefinite, so far as they depend on claims 2 and 15, for the limitation set forth directly above.

5c. Amended claim 25 also stands rejected under 35 U.S.C. 112, second paragraph, for the same reasons as claims 2 and 5, set forth directly above. Claim 25 is vague and indefinite, because it is unclear, how to administer the combination of IL-10 and either the antigen or anti-CD3 into a *T cell*. Appropriate correction is required.

5d. Amended claim 27 is still vague, because it is unclear which T cell precursor that is being referred to? Appropriate correction is required.

Claim 26 is rejected as being vague and indefinite, so long as it depends on claim 25, for the limitation set forth above.

***Conclusion***

6. No claim is allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday, Wednesday-Thursday, 6:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4227 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
July 13, 2003

YVONNE EYLER, PH.D
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